REMARKS

I. Explanation of Amendments to the Specification

Paragraphs within the summary of invention at pages 2-7 and 9-13 have been amended to omit reference to particular claims. According to MPEP § 608.01(d), the purpose of the "Summary of Invention" is to describe the specific invention being claimed in one or more clear concise sentences or paragraphs[1]. As the claims may be amended, canceled and eventually renumbered during prosecution, reference to claim numbers does not provide the most clear and concise description of the present invention. Thus, the Applicants have removed the references to particular claims and have added general language to make these statements more clear and concise. The Applicants have not added new matter to the Summary of Invention.

The application describes two human forms of the Asp2 protease ("Asp2(a)" and "Asp2(b)" splice variants) which differ from each other by the presence or absence of an internal stretch of about twenty-five amino acids. The Applicants believe that they have remained consistent and accurate in their presentation of *the sequences* for these splice variants, *e.g.* in Figures 2 and 3, but have identified inconsistencies in their applications relating to *the names* that are the subject of amendments set forth above.

More particularly, the present application refers to the longer splice variant as "Asp2(a)" and the shorter splice variant as "Asp2(b)." However, the Applicants have identified a few instances in the present application of inconsistencies, *i.e.*, where "Asp2(a)" is used to refer to the shorter splice variant and "Asp2(b)" to the longer. The present amendment eliminates the inconsistencies.

The Brief Description of Figures 2 and 3 contained one such inconsistency, and the amendments at page 16 correct it. Figure 2 plainly depicts the "shorter" Asp2 sequence, and its description has been amended to recite "Asp2(b)" and to cross reference the shorter sequences in the Sequence Listing. The opposite amendment has been made for Figure 3, which plainly depicts the "longer" Asp2 sequence.[2] A similar amendment is made

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[1] The claims recited in the Summary of Invention have been canceled in the Preliminary Amendment dated March 26, 2001.

[2] In the description of Figure 3, the sentence pertaining to denoting the transmembrane domain has been deleted because the Figure lacks brackets and because the transmembrane domain is identified elsewhere in the specification.

at page 35, where the application contains cross-references to Figures 2 and 3. The foregoing amendments ensure that the Specification consistently refers to the "longer" Asp2(a) polynucleotide and polypeptide as having the sequences set forth in SEQ ID NOS: 3 and 4, and the "shorter" Asp2(b) as having the sequences set forth in SEQ ID NOS: 5 and 6.

These amendments are supported by the application as filed because they simply make the terminology more consistent, and the inconsistencies and the manner in which they should be corrected would have been apparent to any reader of ordinary skill in the art.

II. Election

Citing 35 USC §121, the Examiner alleged that claims 151-300 were drawn to 21 distinct inventions:

Group 1, claims 241-250, 254-269 and 279-280, drawn to a method for producing a polypeptide comprising SEQ ID NO: 2, polynucleotides encoding SEQ ID NO: 2, vectors, host cells comprising the same, and the polypeptide comprising SEQ ID NO: 2.

Group 2, claims 151-157, 162-188, 241-249, 251-254-269 and 279-280, drawn to a method for producing a polypeptide comprising SEQ ID NO: 4, polynucleotides encoding SEQ ID NO: 4, vectors and host cells comprising the same, and the polypeptide comprising SEQ ID NO: 4.

Group 3, claims 151-152, 158-160, 162-171, 173-188, 241-249, 254-269 and 279-280, drawn to a method for producing a polypeptide comprising SEQ ID NO: 6, polynucleotides encoding SEQ ID NO: 6, vectors, host cells comprising the same, and the polypeptide comprising SEQ ID NO: 6.

Group 4, claims 151-152, 161-165, 167-169, 173-188, 252, 254-269 and 279-280 drawn to a method for producing a polypeptide comprising SEQ ID NO: 8, polynucleotides encoding SEQ ID NO: 8, vectors and host cells comprising the same and the polypeptide comprising SEQ ID NO: 8.

Group 5, claims 189-195, and 197-200, drawn to a method of identifying agents the inhibit the activity of human Asp2 aspartyl protease (Hu-Asp2) comprising SEQ ID NO: 4.

Group 6, claims 189-194 and 196-200, drawn to a method of identifying agents the inhibit the activity of Asp2 aspartyl protease wherein the hybridization partner comprises SEQ ID NO: 6

Group 7, claim 201, drawn to a method of identifying agents the modulate the activity of Asp2 aspartyl protease wherein the hybridization partner comprises SEQ ID NO: 4.

Group 8, claim 201, drawn to a method of identifying agents the modulate the activity of human Asp2 aspartyl protease (Hu-Asp2) comprising SEQ ID NO: 6.

Group 9, claim 281-292, drawn to a method of identifying agents the modulate the activity of human Asp2 aspartyl protease using SEQ ID NO: 1 and SEQ ID NO: 2.

Group 10, claims 202, 203, 219, 220, 224, 225, 293 and 294, drawn to a method for treating Alzheimer's disease and medicaments thereof.

Group 11, claims 204-218, drawn to a method for assaying modulators of β-secretase activity.

Group 12, claims 221-223, drawn to a method for identifying agents that inhibit the activity of human Asp2 aspartyl protease (Hu-Asp2) using SEQ ID NO: 4.

Group 13, claims 221-223, drawn to a method for identifying agents that inhibit the activity of human Asp2 aspartyl protease (Hu-Asp2) using SEQ ID NO: 6.

Group 14, claims 226-231 and 295-299, drawn to a method of reducing cellular production of amyloid β (Aβ) from amyloid precursor protein using anti-sense reagent.

Group 15, claims 232-240, 270-272 and 274-278, drawn to a polypeptide comprising the amino acid sequence of a mammalian amyloid precursor protein (APP) or a fragment thereof, polynucleotides, and host cells comprising the same wherein the isoform comprises SEQ ID NO: 16.

Group 16, claims 232-240, 270-271 and 273-278, drawn to a polypeptide comprising the amino acid sequence of a mammalian amyloid precursor protein (APP) or a fragment thereof, polynucleotides, and host cells comprising the same wherein the isoform comprises SEQ ID NO: 18.

Group 17, claims 232-240, 270-271 and 273-278, drawn to a polypeptide comprising the amino acid sequence of a mammalian amyloid precursor protein (APP) or a fragment thereof, polynucleotides, and host cells comprising the same wherein the isoform comprises SEQ ID NO: 20.

Group 18, claim 253, drawn to an isolated antibody.

Group 19, claim 300, drawn to a method for the identification of an agent that decreases the activity of a Hu-Asp1 polypeptide.

Group 20, claim 300, drawn to a method for identification of an agent that decreases the activity of a Hu-Asp2(a) polypeptide.

Group 21, claim 300, drawn to a method for identification of an agent that decreases the activity of a Hu-Asp2(b) polypeptide.

In response, the Applicants hereby elect **Group 15**, which includes claims 232-240, 270-272 and 274-278, drawn to a polypeptide comprising the amino acid sequence of a mammalian amyloid precursor protein (APP) or a fragment thereof, polynucleotides, and host cells comprising the same, wherein the isoform comprises SEQ ID NO: 16.

III. The Applicants traverse the restriction of Groups 15 and 16.

The present application is the national stage filing of International Application No. PCT/US99/20881. Unity of invention was determined by the European Patent Office acting as International Examining Authority for the PCT application. The U.S. Patent and Trademark Office must follow this determination and merge the claim groups as set out in the International Preliminary Examination Report.

The claims in Groups 15, 16, and 17 are drawn to polypeptides comprising the amino acid sequence APP or a fragment thereof, wherein the polypeptide further comprises two lysine residues at the carboxy terminus. The claims of Groups 15, 16 and 17 (claims 232-240 and 270-278) correspond to canceled claims 82-90 and 120-128, which were examined by the European Patent Office acting as International Preliminary Examination Authority for International Application No. PCT/US99/20881. In the resulting International Preliminary Examination Report (IPER, attached as Appendix A), the EPO determined that the claims 1-130 were directed to the following two inventions:

1. Polypeptides Asp2(a) of SEQ ID NO: 4 or 8, Asp1 polypeptides of SEQ ID NO: 2, and Asp2(b) polypeptides of SEQ ID NO: 6 and polynucleotides which encode these polypeptides; and

2. An APP isoform wherein the last two carboxy terminus amino acids are lysine residues (claims 82-90 and 120-128).

Therefore, in light of the IPER, there is unity of invention between claims 232-240 and 270-278.

Under PCT Rule 13.2 (as stated in MPEP § 1850), unity of invention exists when "there is a technical relationship among the claimed inventions involving one or more special technical features." The claims of Groups 15, 16 and 17 share the special two lysine residues at the carboxy end of the APP isoform as a "special technical feature." A "special technical feature" is defined in MPEP § 1850 as a "those technical features that define a contribution which each of the inventions considered as a whole, makes over the prior art." The amino acid sequence of APP isoforms *per se* disclosed in the specification, and recited in the claims, were known in the art at the time of filing. It was not known in the art that the addition of two lysine residues at the carboxy end of an APP isoform increases the efficacy of cleavage at the β-secrease site. Therefore, claims 232-240 and 270-278 share a "special technical feature" and the Applicants request that the restriction of Groups 15, 16 and 17 be withdrawn and these claims be examined simultaneously.

CONCLUSION

In view of the forgoing remarks, the Applicants request withdrawal of the restriction requirement in light of Groups 15, 16 and 17.

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Respectfully submitted,

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